

**Amendments to the Claims**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

Claim 1 (withdrawn): A set of libraries of genes which code for proteins which are capable of specific binding interactions with a specific binding partner by amino acid residues at at least two specified positions including a first specified position and at least one other specified position, which set of libraries comprises:

- a) 6 to 20 libraries in which each library has a triplet that codes for at least one but less than 20 amino acids at said first specified position, and is randomized at the or each triplet coding for the said at least one other specified position, the arrangement being such that interactions of the proteins coded for by the said 6 to 20 libraries with a specific binding partner identifies a triplet that codes for an amino acid at the said first specified position that takes part in the specific binding interaction, and
- b) 6 to 20 libraries in each of which libraries said first specified position is randomized and a different one of said at least one other specified positions has a triplet that codes for at least one but less than 20 amino acids.

Claim 2 (withdrawn): The set of libraries of genes as claimed in claim 1, which set of libraries comprises:

- a) 12 libraries in which each library has a triplet that codes for one or several but less than 20 amino acids at the said first determined position, the triplets being as shown in Table 1 or Table 2, and
- b) 12 libraries of corresponding design for each of the said one or more other determined positions.

Claim 3 (withdrawn): The set of libraries of genes as claimed in claim 1, wherein the genes code for zinc fingers.

Claim 4 (withdrawn): The set of libraries of genes as claimed in claim 3, which set comprises 36 libraries in three groups of 12 libraries which code for amino acids at the -1 and +3 and +6 positions respectively.

Claim 5 (withdrawn): The set of libraries of genes as claimed in claim 3, wherein each gene codes for a protein comprising three zinc fingers.

Claim 6 (withdrawn): The set of libraries of genes as claimed in claim 5, wherein each gene codes for a protein having the sequence (SEQ ID NO: 2)

T G E K P Y K C P E C G K S F S X K S X L V X H Q R T H

T G E K P Y K C P E C G K S F S X K S X L V X H Q R T H

T G E K P Y K C P E C G K S F S X K S X L V X H Q R T H

where X is any amino acid.

Claim 7 (withdrawn): A set of libraries of proteins, which proteins are capable of specific binding interactions with a specified binding partner by amino acid residues at at least one specified position including a first specified position and at least one other specified position, which set of libraries comprises:

- a) 6 to 20 libraries in which each library has at least one but less than 20 amino acid residues at the said first specified position and is randomized at the said at least one other determined position, the arrangement being such that interaction of the 6 to 20 libraries with a specific binding partner identifies an amino acid residue at the said first specified position that takes part in the specific binding interaction, and
- b) 6 to 20 libraries in each of which libraries said first specified position is randomized and a different amino acid is present at at least one other specified position.

Claim 8 (withdrawn): The set of libraries of proteins as claimed in claim 7, which set of libraries comprises:

- a) 20 libraries in which each library has one specified amino acid residue at the said first determined position and is randomized at the said one or more other determined positions, and
- b) 20 libraries of corresponding design for each of the said one or more other determined positions.

Claim 9 (withdrawn): The set of libraries or proteins as claimed in claim 7, wherein the proteins are zinc fingers.

Claim 10 (withdrawn): The set of libraries of proteins as claimed in claim 7, which set comprises 60 libraries in three groups of 20 libraries with specified amino acids at the -1 and +3 and +6 positions respectively.

Claim 11 (withdrawn): The set of libraries of proteins as claimed in claim 9, wherein each protein comprises three zinc fingers.

Claim 12 (withdrawn): The set of libraries of proteins as claimed in claim 11, wherein each protein has the sequence (SEQ ID NO: 2)

T G E K P Y K C P E C G K S F S X K S X L V X H Q R T H  
T G E K P Y K C P E C G K S F S X K S X L V X H Q R T H  
T G E K P Y K C P E C G K S F S X K S X L V X H Q R T H

where X is any amino acid.

Claim 13 (withdrawn): A set of libraries of genes which code for the set of libraries of proteins defined in claim 7.

Claim 14 (currently amended): A method of identifying a protein which interacts with a specific binding partner, which method comprises

- (a) providing a set of libraries of proteins ~~as defined in claim 7~~, which proteins are capable of specific binding interactions with a specified binding partner by amino acid residues at at least one specified position including a first specified position and at least one other specified position, which set of libraries comprises:
  - (i) 6 to 20 libraries in which each library has at least one but less than 20 amino acid residues at said first specified position and is randomized at said at least one other specified position, the arrangement being such that interaction of the 6 to 20 libraries with a specific binding partner identifies an amino acid residue at said first specified position that takes part in the specific binding interaction, and
  - (ii) 6 to 20 libraries in each of which libraries said first specified position is randomized and at least one but less than 20 amino acid residues is present at said at least one other specified position,
- (b) incubating the specific binding partner with each library of the set,

- (c) observing specific binding interactions with certain libraries of the set, and
- (d) using the observations to identify a protein which interacts with the specific binding partner.

Claim 15 (original): The method as claimed in claim 14, wherein the specific binding partner is a polynucleotide.

Claim 16 (original): The method as claimed in claim 14, wherein the specific binding interactions are observed by radiometric or luminescent assay.

Claim 17 (original): The method as claimed in claim 14, wherein the specific binding interactions are observed by imaging means.

Claim 18 (original): The method as claimed in claim 14, wherein the specific binding interactions are observed by scintillation proximity assay.

Claim 19 (currently amended): The method as claimed in claim 18, wherein the ~~sets~~ set of libraries of proteins are immobilized on scintillation proximity assay surfaces and the specific binding partner is radiolabelled.

Claim 20 (previously presented): The method of claim 18, wherein after incubation the scintillation proximity assay surfaces are washed to distinguish stronger specific binding interactions from weaker ones.

Claim 21 (withdrawn): The method as claimed in claim 14, wherein the specific binding interactions are observed by colorimetric means.

Claim 22 (withdrawn): The method as claimed in claim 21, wherein the specific binding partner is biotinylated and the specific binding interaction is detected using a signal generating streptavidin conjugate.

Claim 23 (withdrawn): The method as claimed in claim 21, wherein after incubation the binding interactions are washed to distinguish stronger specific binding interactions from weaker ones.

Claim 24 (withdrawn): A protein having the sequence (SEQ ID NO: 1)

T G E K P Y K C P E C G K S F S K K S H L V A H Q R T H  
T G E K P Y K C P E C G K S F S K K S H L V A H Q R T H  
T G E K P Y K C P E C G K S F S K K S H L V A H Q R T H.

Claim 25 (withdrawn): A gene which codes for the protein of claim 24.

Claim 26 (withdrawn): A method of constructing randomized gene libraries in which the number of genes is the same as the number of encoded proteins and which contain no termination codons at the predetermined positions of randomization, the method comprising the steps of:

- a) providing a template oligonucleotide which is fully randomized at predetermined codon positions;
- b) for each predetermined codon position providing a pool of selection oligonucleotides, wherein each member of said pool contains a different codon selected from the group comprising:  
AAA, AAC, ACC, AGC, ATG, ATT, CAG, CAT, CCG, CGC, CTG, GAA,  
GAT, GCG, GGC, GTG, TAT, TGG, TGC, TTT.  
at the predetermined codon position;
- c) selecting one or more selection oligonucleotides from each pool in order to encode the required gene or library;
- d) allowing the ligated selected oligonucleotides from each pool to hybridize with the template oligonucleotide;
- e) forming one or more constructs by ligating the hybridized selection oligonucleotides together;
- f) removing a region from a gene of interest corresponding to the hybridized product from step e);



- g) forming a gene library or genes by ligating the products from step e) into the said gene of interest wherein the said gene of interest is contained within a suitable expression vector.

Claim 27 (withdrawn): A method of producing proteins encoded by the randomized gene libraries of claim 26 comprising the steps of:

- a) transforming a suitable host cell with the gene or gene library of claim 26 construct;
- b) expressing the genes to form proteins;
- c) purifying the proteins.

Claim 28 (new): A method of identifying a protein which interacts with a specific binding partner, which method comprises

- (a) providing a set of libraries of proteins, which proteins are capable of specific binding interactions with a specified binding partner by amino acid residues at at least one specified position including a first specified position and at least one other specified position, which set of libraries comprises 60 libraries in three groups of 20 libraries with specified amino acids at the -1 and +3 and +6 positions respectively.
- (b) incubating the specific binding partner with each library of the set,
- (c) observing specific binding interactions with certain libraries of the set, and

Appl. No. 09/787,228  
Amendment dated January 20, 2006  
Reply to Office action of September 20, 2005

- (d) using the observations to identify a protein which interacts with the specific binding partner.